EDITORIAL

Is Sepsis a Cardiac Nemesis? Exploring New Vistas

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Septic shock is an important cause of morbidity and mortality in patients admitted to intensive care units, especially amongst the pediatric population.[1–4] Many patients have concomitant cardiac dysfunction that can manifest as clinical heart failure, recurrent arrhythmias causing hemodynamic instability, and eventual end organ damage. It is clinically relevant to have a reliable, easily measurable, and reproducible biomarker that can help predict outcomes amongst patients with septic shock. Elevated cardiac biomarkers which are well-known predictive markers in patients with acute coronary syndromes may fulfill these criteria and serve as prognostic surrogates in patients with septic shock.[5–8]

In this issue, Baranwal et al.[9] report on their experience of using creatine kinase-MB isoenzyme (CK-MB) as a potential biomarker for myocardial dysfunction in pediatric septic shock. Among 80 children (aged 3 months to 12 years), 40 each with nonshock sepsis and septic shock survivors (SSS), pediatric logistic organ dysfunction (PeLOD) score, vasoactive inotrope score, CK-MB, and echocardiographic measures of myocardial function were recorded on days 1, 3, 7, and 10. All patients underwent a repeat echocardiography at 1 month. The authors report that SSS patients had a higher CK-MB and PeLOD score and more frequent occurrence of myocardial dysfunction. Reduction in CK-MB over 10 days correlated well with improvement in PeLOD and echocardiographic measures of myocardial function among SSS. At 1-month follow-up, all had normal echocardiographic parameters. The study concludes that SSS patients had a markedly elevated CK-MB and reduction mirrored the improvement in clinical status and myocardial function. The authors finally postulate that CK-MB could be a potential monitoring tool for septic cardiomyopathy in settings with limited resources.

This study adds to our existing knowledge about the association of elevated cardiac biomarkers in septic shock, especially in the Indian context. Previous studies have also confirmed that higher cardiac biomarkers are associated with increased mortality in septic shock, although the current study did not comment on any link with mortality.[10–13] Surprisingly, Baranwal et al. mention that survivors and nonsurvivors of septic shock were similar in terms of their CK-MB levels (180.8 ± 110.2 vs 161.9 ± 40.9; $p = 0.5$) and echocardiographic parameters. Whether this was due to the small number of patients in the current study precluding any meaningful correlation with mortality (even if one existed) or due to the fact that only CK-MB (and not troponin) was assessed, needs to be substantiated in studies with a large number of patients.

Although many studies have commented on the left ventricular (LV) systolic function in patients with septic shock, diastolic function is often overlooked despite being a very important part of echocardiographic assessment in such patients,[14–17] and therefore Baranwal et al. deserve credit for a detailed evaluation of both systolic and diastolic functions of the LV. The authors assessed ejection fraction [left ventricular ejection fraction (LVEF)], fractional area change (FAC), fractional shortening, and E/A ratio (EAR). The systolic function parameters were below the accepted normal cutoffs in 25%, 45%, and 15%, respectively, while diastolic dysfunction was seen in 12.5%. Overall, more than half (55%) had at least one echocardiographic parameter of myocardial dysfunction. However, a close analysis of the data reveals that in this study, amongst patients of SSS with myocardial dysfunction, the reported mean LVEF was 50.05 ± 6.1, FAC 33.4 ± 4.3, and EAR 0.84 ± 0.07, values which are not significantly different from normal, when one takes into account the mean $\pm$ SD values. Future endeavors in the field could perhaps therefore focus on more sensitive echocardiographic parameters, such as global or regional ventricular strain analysis for systolic function and tissue Doppler imaging or pulmonary vein Doppler imaging for diastolic function analysis.

Two other key areas deserve further attention in this patient population. Electrocardiogram and echocardiography rarely demonstrate ischemia or regional wall motion abnormalities, respectively, and only a minority has inducible ischemia on subsequent stress testing or occlusive coronary artery disease. The mechanistic explanation of the reversible rise in cardiac biomarkers in septic shock is multifactorial including direct cardiac myotoxic effects due to the release of endotoxins, free radicals, and catecholamines, myocardial ischemia due to coronary microembolization, demand–supply mismatch, and in extreme cases, cardiac apoptosis. Further research needs to focus on the exact etiopathogenesis of elevated cardiac biomarkers in patients with septic shock.

Second, one needs to define which particular cardiac biomarker to study in patients with septic shock, viz., only CK-MB (as done in the current study) or troponins (as described in most of the previous reports), with the introduction of hs-cTn further enhancing diagnostic sensitivity.[7,10,17,18] An advantage of using multiple biomarkers is to be able to document if diverse markers (CK-MB, troponins, C-reactive protein, etc.) have differential release kinetics and develop cutoffs for them to predict outcomes. Heterogeneity in earlier data has often been due to variability in the timing of measurement, type of assay used, and hemodynamics at the time of assessment, necessitating the need for clarifying these issues before routinely using a serial biomarker estimation in clinical practice.

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